

# **EXHIBIT 23**



# U.S. Department of Labor Occupational Safety & Health Administration

**www.osha.gov**



Search



Advanced Search | A-Z Index

Regulations (Preambles to Final Rules)

## Section 5 - V. Health Effects

◀ [Regulations \(Preambles to Final Rules\) - Table of Contents](#)

- **Record Type:** Occupational Exposure to Asbestos, Tremolite, Anthophyllite and Actinolite
- **Section:** 5
- **Title:** Section 5 - V. Health Effects

## V. Health Effects

In its proposal OSHA reviewed the available health effects evidence and preliminarily concluded that "there are a number of studies which raise serious questions about the potential health hazard from occupational exposures to non-asbestiform tremolite, anthophyllite and actinolite. However, the currently available evidence is not sufficiently adequate for OSHA to conclude that these mineral types pose a health risk similar in magnitude or type to asbestos. The Agency believes, however, that the evidence suggests the existence of a possible carcinogenic hazard and other impairing non-carcinogenic adverse health effects." (55 FR 4943).

After reviewing the rulemaking record compiled subsequent to the publication of the proposal, OSHA reaffirms its view of the health effects evidence. The few new studies that have come to light in this rulemaking are still inconclusive. It should be noted that OSHA believes the health effects evidence falls short regardless of whether this proceeding is viewed as deregulatory or as a regulatory initiative.

More specifically, OSHA believes that the evidence viewed as a whole does not rule out a possible carcinogenic effect of certain subpopulations of non-asbestiform ATA at an unspecified exposure level. However, as discussed below, various uncertainties in the data and a body of data showing no carcinogenic effect, do not allow the Agency to perform qualitative or quantitative risk assessments concerning occupational exposures. Further, the subpopulations of non-asbestiform ATA which, based on mechanistic and toxicological data, may be associated with a carcinogenic effect, do not appear to present an occupational risk. Their presence in the workplace is not apparent from the record evidence.

### 1. Human Studies

#### Summary

The epidemiologic studies submitted to this record consisted of no studies which were not available to OSHA at the time of the proposal. The interpretations submitted in comment and testimony also reiterated positions taken prior to the proposal, although participants expanded on them. Additional analyses concerning reported cases of cancer in the NIOSH study cohort were submitted, both in support of the position that the talc exposure was correlated to cancer, and in support of the opposing view that smoking was a likely cause of any elevated SMR.

A review of the human studies in the record follows: Where no new interpretative comment was offered, only a summary describes it. Where new comment or updated data was

submitted, a discussion is presented. The discussion is organized around the categorization of the minerals to which the cohorts were exposed. As discussed at length in the proposal, uncertainty about the content of the mineral exposure at times made definitive interpretation difficult. However, because the substances to which workers are exposed are mixed, OSHA believes that mixtures can be evaluated in their own right. If disease cannot be correlated to exposure to a specific mineral in a mixed mineral product, then prudent health policy allows OSHA to ascribe causation to the mineral mixture, rather than to any component.

a. Studies of exposures to ATA and asbestos contaminated ores.

As OSHA noted in its proposal, McDonald et al (Ex. 410-6) reported an excess of respiratory cancer including mesotheliomas, among vermiculite miners in Libby, Montana. Vermiculite, a mica - like mineral ore, was contaminated with four to six percent tremolite-actinolite fibers. Mineralogic analysis of the Libby mine's ore showed the fibers to be mostly an asbestiform type of fiber. However there were also "massive amphibole crystals, which when pulverized produced cleavage fragments resembling fibers"(p.439). OSHA noted, "[a]lthough the fiber analyses indicate that some of the particles were non-asbestiform in origin, the predominant fiber exposure appears to be from asbestiform tremolite. ...Standardized Mortality Ratios(SMRs) were computed for the cohort of 406 Men. When compared to death rates of men in the U.S., there was a substantial excess number of deaths from respiratory cancer (SMR=245). Four of the 43 deaths were from mesothelioma. There was also a substantial excess number of deaths from non-malignant respiratory disease(SMR=255). There was no excess number of deaths from cancers of non-respiratory sites. When compared to the death rates of Montana men, the cohort's excess mortality was even greater; for example the SMR for respiratory cancer rose from 245 to 303." OSHA stated in the proposal that the result of the Libby, Montana study and other studies of workers exposed to tremolite asbestos contaminated ores "provide additional evidence on the high potency of asbestiform tremolite. Although non-asbestiform tremolite was present it is not possible, from the data presented, to discern what contributing effect the non-asbestiform minerals may have had."(55 FR 4944).

Most comment and testimony during the rulemaking concerning the Libby Montana study reiterated OSHA's earlier analysis. The American Thoracic Society pointed out that the mineralogic characterization of the Libby deposit as containing tremolite asbestos has been challenged, and for that reason and because this is a "non-replicated" study, warned against relying on it.(Ex. 525, p. 5) Dr. Nicholson, in his testimony, pointed out that the presence of non-asbestiform minerals in the deposit, made the study compatible with the risk expected on the basis of measured fiber concentrations (Tr. 5/8, p. 55). NSA noted that "the Libby vermiculite workers were exposed to asbestiform tremolite and asbestiform actinolite and thus this study is not useful in the examination of the non-asbestiform ATA question." (Ex. 524, p. 26.) As stated in the preamble to the proposal, OSHA believes that the results of the Libby, Montana study, and other studies where miners were exposed to both asbestos tremolite and non-asbestiform tremolite (see e.g. Kleinfeld et al, Ex. 84-402 and Brown et al (Ex. 84-25) provide additional evidence on the high potency of asbestiform tremolite. Although non-asbestiform tremolite was present it is not possible from the data presented, to discern what contributing effect the non-asbestiform minerals may have had to the excess cancer observed in this study.

b. Studies of exposures to mixtures of other non-asbestiform analogues with non-asbestos minerals.

The Homestake gold mine study (Ex. 84-45, Docket H-033c) was a retrospective cohort mortality study of 3328 gold miners who worked in full-time underground jobs for at least one year between 1940 and 1965. There were 861 observed versus 765 expected deaths overall. The primary exposures were to amphibole minerals in the cummingtonite-grunerite

series (the non-asbestiform analogue of amosite) and silica. According to the study's investigators "no association, as measured by length of employment underground, dose (total dust x time), or latency was apparent with lung cancer mortality (43 observed vs. 43 expected). However Dr. Nicholson noted that the conclusion of no excess lung cancer risks associated with exposures at the mine was based on calculations using U.S. mortality rates, rather than South Dakota mortality rates. Had South Dakota mortality rates been used, SMRs would have been raised to 160, rather than the 100 reported by the investigators.(Tr. 5/8, p. 81-2). Dr. Bob Reger who testified for the American Mining Congress (AMC) suggested that such an adjustment is improperly made without adjusting for age (See Tr. 5/8, p. 82). Although OSHA believes that uncertainty in interpretation is introduced by the study's use of U.S. mortality rates, reconstruction of the SMRs applying the South Dakota mortality rate is hindered by the lack of data which would allow an age specific reconstruction. Dr. Nicholson also noted that the Homestake results were not incompatible with an asbestos effect, because in the longer duration category there is a total of only three deaths, an additional uncertainty, and there is a possibility that one has individuals that are survivors and "...demonstrate a lower risk by virtue of the fact that they could have had lesser exposure jobs, and, thus, be at lesser risk ..."(Tr. 5/9, p. 83). OSHA believes Dr. Nicholson's comments correctly state some of uncertainties of the study, i.e., small number of deaths, and the possibility that retirees can be a survivor population. These uncertainties do not, by themselves, provide a basis for interpreting the Homestake studies as confirming evidence for the carcinogenic effect of non-asbestiform minerals. The study is not inconsistent with a positive association and does not prove that there is no association. However, it can also not be interpreted as clear evidence of association.

Other studies concerned two groups of iron ore miners and processors, who were exposed to taconite dust which may have contained cleavage fibers of the cummingtonite-grunerite series (Higgins et al., 1983 (Ex. 410-18); Cooper et al., 1988 (Ex. 427)). OSHA agrees with the analysis of all participants who commented on these studies, to the effect that they do not inform as to the carcinogenicity of non-asbestiform ATA, perhaps because of the low exposures in one mine and the lack of latency to observe lung cancer in the other (See e.g. NSA's post hearing brief (Ex. 524 p.27), Dr. Nicholson's testimony (Tr. 5/8, pp. 55-56)).

In its proposal OSHA described at considerable length the studies of the New York State tremolitic talc miners and millers, which had been undertaken by NIOSH. The entire preamble discussion is incorporated here (see 55 FR 4946). One significant interpretive issue concerns the mineral content of the deposit and thus the employees exposures. Vanderbilt testified that "the ore composition is fairly consistent...the content of the talc being between 20 to 40 percent, serpentine, 20 to 30 percent; the tremolite 40 to 60 percent, the anthophyllite between zero and five (percent), and ...quartz...in very trace amounts." (Tr. 5/11, p.103). Testimony in the record supports Vanderbilt's claim that any of the asbestos minerals that falls into the scope of this standard is not a component of the ore. (See Langer et al, and Dunn GeoScience in the prehearing submission of the American Mining Congress and the NSA, Ex. 479-6, 479-23; R.J. Lee in the Vanderbilt Dust Project, Ex. 433). While the reports of these analysts find no evidence of the six asbestos types in the Vanderbilt talc mines, all three noted the presence of asbestiform talc fibers and "transitional particles". These are the same "transitional particles", described earlier in the section on Mineralogic Considerations, which resemble asbestos and talc but are not technically asbestos. NIOSH reiterated its original evaluation that the Vanderbilt deposits contained asbestiform as well as non-asbestiform tremolite and anthophyllite. (See Tr. 5/9, p. 11.) OSHA notes that the debate over the mineralogic content of the Vanderbilt mines remains unresolved. OSHA believes however that the presence of asbestiform talc and the so called "transitional particles" together with the undisputed presence of non-asbestiform tremolite and anthophyllite may have led to the identification of various particles as asbestiform tremolite and/or anthophyllite.

Various industry and government sponsored reviews and updates of NIOSH's study have been conducted. In the NPRM, OSHA concluded that "the NIOSH studies provide evidence to support the possibility that exposure to minerals at the mine is correlated to the excess mortality from lung cancer and nonmalignant respiratory disease and an excess of pleural thickening and lung decrements. However due to uncertainties in the mineral content and mixed mineral contents, the study does not show that it is more likely than not that non-asbestiform fibers are the cause of the disease."(55 FR 4947).

A former NIOSH researcher, Dr. John Gamble, who has criticized basing the regulation of ATA as asbestos on the NIOSH study, submitted additional material to substantiate his contention that attributing excess cancer to non-asbestiform ATA was speculative (Ex. 478-8). Gamble performed an update and re-evaluation of the 1980 NIOSH study in which he added eight more years of follow-up, an exposure latency analysis, and a nested case-control study to control for smoking and other occupational exposures. In his analysis Gamble found a significant increase in mortality for all cause (SMR=128), all respiratory diseases (SMR=251), all malignant neoplasms (SMR=145), and lung cancer (SMR=207). The lung cancer SMRs were elevated in the 20-36 year latency group (SMR=258) and for workers with less than one year tenure at the mine (SMR=357). In the nested case-control study Gamble found no apparent increased risk associated with non-Vanderbilt jobs. However he did find that the odds ratio for cases who smoked was six times that of combined ex-smokers and nonsmokers. Gamble stated in his conclusions that "Although lung cancer SMRs are elevated, we could not find an exposure-response relationship. The lack of an increase risk of lung cancer is consistent with other mining populations exposed to non-asbestiform minerals. The time occurrence of lung cancer is consistent with a smoking etiology." (Ex. 478-8, p.2) NIOSH has stated that Dr. Gamble's opinions "are his alone; arise from activities he performed which, in part, created the appearance of a conflict of interest; and represent conclusions, as judged by independent reviewers, which are not supported by data."(Ex. 520, p. 3). NIOSH continues to support the findings of it earlier studies in the New York talc mines, which, they concluded, provide clear evidence of an increase in lung cancer and other asbestos related disease in talc workers. (Ex. 478-15, Tr. May 8, p. 24) In its post hearing comments NIOSH submitted an update of the Gouverneur Talc study which added eight new lung cancers to the ten identified in the earlier report (Ex. 532). According to NIOSH the SMR for lung cancer was uniform across tenure strata and increased with increasing latency. There was a statistically significant excess in lung cancer in those with 20 years of more latency and with less than one year employment. Those in this latency group with greater than one year duration also exhibited an increased risk but it was not statistically significant. The increased risk of lung cancer among those with short duration also was observed in the 1989 analysis. (Ex. 532 at p.5). NIOSH offered three explanations: cohort members may have been employed in other New York State talc mines and mills where there may have been additional exposures to the same or to similar types of mineral dust and noted that it is known that half of the lung cancer cases worked on other talc mining operations; some of the short duration group may have had very high exposures; and smoking habits among the employees may have been different from the reference population. However, NIOSH performed an exercise to show that differences in smoking could not account for the observed increase in lung cancer. NIOSH calculated SMRs assuming that 100 percent of the cohort were smokers. NIOSH noted that the SMR for lung cancer would have been only 160, instead of 207. In addition, the updated results show the SMR for non-malignant respiratory disease was significantly elevated among those with more than one year of tenure(SMR=290, CI 144, 518). The types of nonmalignant disease observed in this study is not known to be smoking related.

OSHA notes, however, that virtually no other participant endorses the NIOSH study as a basis for regulation. For example, the ATS report noted that the results of the case-control study and the lack of any dose-response relationship for lung cancer risk in the cohort study do not support a conclusion that the elevated risk in this population was attributable to mine

exposures.(Ex. 525, p. 6) Dr. Richard Morgan, testifying for the NSA, stated that "Even if subsequent studies of the Vanderbilt mine permit a conclusion that an occupational exposure at the mine contribute to the risk, there will remain the problem of deciding which exposures (among many) are likely responsible. At this time, however, there is no evidence from these studies that will permit any conclusion concerning non-asbestiform ATA." (Ex. 490C, p. 180).

In summary, OSHA believes that the epidemiological studies, as a whole, provide insufficient evidence to inform as to the carcinogenicity of non-asbestiform ATA. For example, epidemiological studies involving exposures to non-asbestiform amphiboles other than non-asbestiform ATA are hindered by low "fiber" counts and short latency periods. It is likely that even if exposures had been to "true" asbestos, a positive response would not have been observed under similar low dose, low latency conditions. Epidemiological studies of upstate New York talc miners are hindered by the fact that workers were exposed to a mixture of minerals (the identification of which is still somewhat at debate). Although plausible arguments have been presented that suggest that the increase in lung cancer is consistent with a smoking etiology, OSHA believes that it is also likely that exposures at the mine are responsible for the observed disease, especially in the case of nonmalignant respiratory disease. Nevertheless, due to the mixed mineral exposures OSHA concludes that it is not possible from the present data, to determine what role the non-asbestiform ATA may have played in the induction of that disease.

## 2. Lung Burden Studies

In the proposal OSHA discussed the findings of several lung burden studies. One study discussed the case study of a mesothelioma death in which an analysis of the autopsied lungs showed elevated levels of tremolite (Ex. 410-10). The fibers of tremolite were of low aspect ratio (i.e. 7:1) and OSHA concluded that low aspect ratio tremolite appeared to have contributed to the induction of mesothelioma (55 FR 4944). However, Mr. Kelly Bailey, testifying for the NSA, took issue with OSHA's conclusion noting that this study involved only a single case study of an individual who was also exposed to chrysotile and the authors of the report stated that the possible effects of tremolite are uncertain. Mr. Bailey also noted that the tremolite "present in the lungs of this case had a mean aspect ratio of 7:1" and "... it is obvious that a distribution of asbestos fibers were found, many with aspect ratios greater than 20:1" (Bailey testimony, Ex. 479-23).

In the proposal OSHA also discussed lung burden studies among miners exposed to both chrysotile and tremolite (Rowlands et al., Ex. 84-178; McDonald et al., Ex. 84-175; Glyseth Ex. 312). These studies indicated that despite high exposure levels of chrysotile, analyses of autopsied lungs showed higher lung burdens of tremolite. OSHA concluded however that the fact that there were was a mixture of mineral fiber types precluded one from ascribing causation to one particular mineral type.

The American Thoracic Society (ATS) reviewing the same studies concluded that "although the role of chrysotile versus tremolite in producing disease in these patients could not be clearly sorted out, the ...data appear to indicate that fairly low aspect ratio fibers of tremolite are capable of causing disease, probably in fairly low concentrations in the case of pleural plaques, but certainly only in very high concentrations in regard to mesothelioma and asbestosis" (Ex. 525, p. 10).

In response to the ATS report, Dr. Arthur Langer, a mineralogist, noted that the "fairly low aspect ratio fibers of tremolite" referred to in the ATS report involve fibers measurements made counting all fibers (i.e. not only those greater than 5 micrometers) and using geometric means. Langer states that "geometric means can be very misleading and the raw data are needed. If one only counts the fibers longer than the 5 um geometric mean, the aspect ratio of

the tremolite fibers is greater than 20:1." Dr. Langer adds that "the data from Canada are problematic in that there is a mixed population of tremolite (when present) which skews size distribution in lung burden studies towards short wide 'fibers'. The disease (plaques) may have been caused by thin fibers (asbestos) at the pleura. The thick cleavage fragments in the lung parenchyma may have little to do with the disease process at the pleura" (Ex. 529-7, pp. 15-17).

Lung burden analyses were also performed by Dr. Jerrold Abraham, a physician and pathologist at the State University of New York. In his testimony and written comments to the proposal, Dr. Abraham presented his analyses of the lung tissues of deceased talc miners from upstate New York. Dr. Abraham testified that these analyses showed that the lungs of these talc miners included both asbestos and non-asbestiform minerals, despite the fact that the talc miners are claimed by some parties to be exposed to only non-asbestiform tremolite. (Tr. May 10, p. 119).

However several hearing participants objected to Dr. Abraham's analyses (See Morgan and Reger for the American Mining Congress, Ex. 508; Langer et al., Ex. 511; and the R.T. Vanderbilt Co., Ex. 513). In summary, these commentators stated that the review and analyses of the talc miner cases lacked documentation and included neither smoking histories nor prior occupational exposures. They suggested that these cases may have had heavy smoking histories or prior exposure to asbestos which could have induced the observed disease. In particular Dr. Langer, a mineralogist, stated that the "limitations of the report are so great that the data are reduced to anecdotal observations" (Ex. 511).

OSHA acknowledges the limitation of these analyses. However, the finding of a rare disease such as mesothelioma, among a group of miners exposed to mixed mineral environments, raises concern over these type of exposures. Furthermore smoking is not known to induce mesothelioma. However, as was stated in the case of the Canadian chrysotile miners, the mixture of mineral types precludes one from ascribing causation to non-asbestiform minerals. This problem, in addition to the uncertainties involved in Dr. Abraham's analyses, do not provide sufficient information to conclude that non-asbestiform ATA present a risk similar in magnitude or type to asbestos.

In summary, lung burden analyses indicate that non-asbestiform minerals are present in the lungs of cases diagnosed with lung cancer and mesothelioma. Several arguments have been put forth by hearing participants both for and against the implication that non-asbestiform contributed to the observed disease. OSHA believes that it is difficult to discern what contributing effect the non-asbestiform minerals may have had because other asbestiform minerals are also present.

### 3. Animal Studies

#### a. Mechanistic studies

OSHA noted in the proposal that several studies in the record suggested that fiber dimension is an important factor in asbestos-related disease development. (55 FR at 4944). Dr. Merle Stanton's landmark study (Stanton et al.(Ex. 84-195, Docket H-033c)) is generally accepted as showing that fiber dimension is an important determinant in mesothelioma production. Dr. William Nicholson, testifying for OSHA described Stanton's study in his testimony. "Seventy-two separate experiments were conducted with different mineral materials, including the commercial asbestos varieties, man-made mineral fibers and minerals containing varying other percentages of fibers. The results of those studies indicated, and his major conclusion was, that the length and diameter of the fibers were the most important factors determining carcinogenicity. Longer fibers were more carcinogenic than shorter ones, and thinner ones more so than thicker ones..." (Tr. 5/8, p. 40).

Most comment and testimony acknowledged that Stanton's work demonstrated that fiber dimension is generally related to tumor production. (See e.g. NSA's post-hearing brief at 19, Ex. 524; Dr. Oehlert's testimony Tr. 5/9, p. 88) For example, Dr. Oehlert, a statistician testifying for NSA stated "In agreement with Stanton, I find that the log number of index particles per microgram in a sample is the best single predictor of tumor probability for that sample. The index particles -- I believe the term was coined by Stanton -- are those particles longer than 8 micrometers and narrower than .25 micrometers." (Tr. 5/9, p. 88).

However, participants disagreed over more specific interpretations of Stanton's study. For example Dr. Nicholson (Ex. 484, Tr. 5/8), NIOSH (Ex. 478-15, Tr. 5/9), and Dr. Groth (Tr. 5/10) asserted that Stanton's work showed that all fibers with certain dimensions had tumorigenic potential; that the greatest correlation existed between fibers of a diameter less than .25 micrometers and greater than 8 micrometers (the "index particles"), but that even a size dimension of 4 to 8 micrometers in length, with a diameter of .25 to 1.5 micrometers had a correlation coefficient of .45. (See e.g. testimony of Dr. Nicholson, 5/8 at 41).

The NSA, in its cross-examination and post-hearing submissions, challenged the interpretation that Stanton's studies show that fibers with aspect ratios as low as 3:1 or 5:1 increase tumor response stating:

During the hearing testimony, the fact that all of the studies involved exposures to a population of fibers or particulates was consistently agreed upon. This fact does not allow one to attribute a specific aspect ratio or dimension as the cause of a response in these animal studies... It is important to recognize that the entire particle size profile of the exposure (width, length, and aspect ratio distribution) contributes to the results of any study. When one looks at the particle width, length, and aspect ratio distributions of cleavage fragments and compares these same distributions to those for asbestos, the population characteristics are easily seen to be quite different...(NSA, post-hearing brief, Ex. 524 at 16).

Various statistical analyses of Stanton's studies were submitted. The study cited as supporting low aspect ratio toxicity, is Bertrand and Pezerat (Ex. 84-114, Docket H-033c)). OSHA described this study in its proposal as finding "a high correlation between aspect ratio and tumor probability for durable minerals. In their analysis tumor probability began to rise at aspect ratios of about 3 to 5". (55 FR at 4944). However, the Bureau of Mines stated in their comments that OSHA did not fully describe Bertrand and Pezerat's findings. They pointed out that "the slope of the curve was extremely small at 3:1 to 5:1 aspect ratios and aspect ratios of 3:1 to 5:1 represent about 5 percent probability (base level in the study)" and "No indication was given as to whether 5 percent is statistically significant to control populations." (Ex. 478-6) Similarly the NSA stated that since Bertrand and Pezerat's "analyses deal with distributions of aspect ratios, it is inappropriate to suggest that an aspect ratio of three or five or any specific value is the reason for the carcinogenic response". (Ex. 524, p. 22) NSA's witness, Dr. Gary Oehlert presented a statistical reanalysis of Stanton's data. Dr. Oehlert stated that his analysis showed that the log number of index particles was the most significant predictor of tumor probability and once index particles have been accounted for, aspect ratio has no further predictive information to provide. (Tr. 5/9, p. 90). However, it should also be noted that although Dr. Oehlert concluded that the number of index particles is the "best" predictor of tumor probability, his analyses also show that aspect ratio is statistically significantly correlated to tumor probability. Dr. Oehlert suggested that this correlation is likely due to the fact that aspect ratio is related to the number of index particles. Nevertheless he states that nonindex particles may contribute to carcinogenicity, but that the Stanton data are not precise enough to determine their influence. In addition, Dr. Oehlert noted that the mineral type is a significant predictor of tumor probability... and should be included when estimating tumor risk. (Tr. 5/9 at 2-87).

Dr. David Groth, a pathologist, testifying on his own, concluded from his review of Stanton's



work that "the results of these studies (i.e. Stanton's) clearly document the importance of fiber size and the induction of cancer by fibers. They also indicate that the chemistry and crystalline structure of the fibers play either no role or a secondary role in the induction of cancer by fibers." Dr. Groth stated that "the results of these experiments have not been seriously challenged by data derived from other animal experiments, and remain as valid today as they were in 1981"(Tr. 5/10, pp. 30-31).

Other dimensional hypotheses were also submitted to the record. Dr. Morton Lippman's 1988 paper which, after reviewing various human and animal studies, identified dimensional ranges for different health effects, was submitted by NIOSH (Ex. 478-15) and others (NSA, Ex. 479-23; AMC, Ex. 479-6). Based on his review of animal injection studies and human lung analyses, Dr. Lippman concluded that the various hazards associated with asbestos (i.e. asbestosis, mesothelioma and lung cancer), are associated with critical fiber dimensions and these dimensions are different for each disease. For example, Dr. Lippman concluded that asbestosis is most closely associated with the surface area of fibers with lengths greater than 2 micrometers (um) and widths greater than 0.15 um; mesothelioma is most closely associated with the number of fibers with lengths greater than 5 um and widths less than 0.1 um; and lung cancer is most closely associated with the number of fibers with lengths greater than 10 um and widths greater than 0.15 um.

The data in the record support and OSHA concludes that fiber dimension is certainly a significant determinant of biological function. OSHA also concludes that despite the various re-analyses of the Stanton study, the basic premise of this study still holds true, that is, that tumor probability increases with the number of long and thin durable particles. However the data available are not precise enough to determine at what point there is no significant carcinogenic potential.

OSHA further concludes that longer, thinner fibers are likely to be more pathogenic. The evidence shows that dusts containing cleavage fragments, rather than asbestiform material, contain substantially fewer longer thinner particles. Thus, a dimensional theory of pathogenicity does not by itself demonstrate that non-asbestiform ATA has similar health effects to asbestos. Even if dimension were the principal determinant of biologic potential for mineral dusts, the evidence in this record is not sufficient to allow OSHA to draw the line for regulation for non-asbestiform ATA at specific dimensions.

#### b. Empirical Studies

OSHA stated in the proposal that the empirical studies in animals are not sufficiently supportive of the mechanistic information to conclude that the risks are similar in magnitude and type for both asbestiform and non-asbestiform minerals.(55 FR at 4946). Although OSHA discussed a preliminary report of early results in its proposal, the one totally new study submitted to the record concerned intraperitoneal injection studies in rats of six samples of tremolite of different morphological types conducted by a Scottish team consisting of John Davis, John Addison and others. Dr. Addison testified at the hearing and submitted both draft and final papers describing the experiment (Ex. 479-22; Tr. 5/11). In this study six different samples of tremolite of different morphological types were prepared as dusts of respirable size and used in intraperitoneal injection studies in rats. Three samples were identified as being tremolite asbestos (California, Korean and Swansea samples). A fourth sample, called Italian tremolite, was initially identified to be non-asbestiform but was later identified, after the tumors were observed, as a "brittle type of fibrous tremolite". The two remaining samples were identified as non-asbestiform tremolite (Dornie and Shinness samples). The three asbestiform tremolite samples produced mesotheliomas in almost all animals tested (California, 100 percent; Swansea, 97 percent; and Korean, 97 percent). The Italian sample which had "relatively few asbestos fibers" produced mesotheliomas in 67 percent of the animals tested although at significantly longer induction periods. The two

remaining samples produced "relatively few tumors" (Dornie, 12 percent and Shinness 5 percent) and were considered, by Dr. Addison to be within the range of background incidence of mesotheliomas observed in historical controls in his lab.

Table 1. Summary of survival data and fiber number for 10 mg dose

Sample	#animals	#mesoth- eliomas (percent)	Median survival time (days)	# fibers (10(5))/mg	#fibers (10(5))/mg len> 8 um dia.< .25
Calif.....	36	36 (100)	301	13430	121
Swansea.....	36	35 (97)	365	2104	8
Korea.....	33	32 (97)	428	7791	48
Italian.....	36	24 (67)	755	1293	1
Dornie.....	33	4 (12)	*	899	0
Shinness....	36	2 (5)	*	383	0

\* Not calculated, table extracted from Davis et al. (Ex. 479-22)

From these results Dr. Addison concluded that all the samples possessed some potential to produce mesotheliomas. However he pointed out two apparent anomalies. One, the Swansea sample had fewer fibers than the Korean sample but both produced a maximum response. Dr. Addison explained that one possible explanation may be that the relationship between fiber number and mesothelioma production is blurred by the overdose situation (i.e. a saturation effect). The second anomaly noted by Addison was the difference in fiber number and mesothelioma production between the Italian and Dornie samples. From Table 1 above, as presented in the Addison study, the Italian sample had 1293 x 10<sup>5</sup> fibers/mg and the Dornie had 899 x 10<sup>5</sup> fibers/mg. Dr. Addison notes however that when only those fibers from this group (i.e. fibers with aspect ratios > 3:1) which have lengths greater than 8 um are counted, the Italian sample had 1/3 fewer fibers but produced a higher percentage of tumors (See for example Tables 2(d) and 2(e), Ex. 470-22). Addison also states that while "it is true that many of the long fibers in the Dornie specimen were greater than 1 um in diameter...if only fibers greater than 8 um in length and less than 0.5 um in diameter were considered, the two specimens have approximately equal numbers which still does not conform to their very different carcinogenic potential." (Ex. 479-22, p 13).

This study was interpreted differently by various participants. The NSA and National Aggregates Association's joint submission found the results of the Davis et al study consistent with its position that "the higher the proportion of tremolite federal fibers (i.e. particles with aspect ratios > 3:1) with widths less than 0.5 um, the greater the incidence of tumors. Conversely, the higher the proportion of tremolite federal fibers with widths greater than 1 um, the lower the incidence of tumors." (Ex. 529-8, p. 3). The NSA in its post hearing comments further stated that the Davis et al data "showed an absence of excess tumors from non-asbestiform ATA, and that the best parameter to explain the formation of tumors was the number of >32:1 aspect ratio Stanton particles, not 3:1 cleavage fragments." (Ex. 524, p.2) NIOSH found that the Davis et al study showed that all forms of tremolite asbestos should be considered carcinogenic, and that it presents no clear evidence indicating that non-asbestiform tremolite is not carcinogenic. However NIOSH expressed serious concerns about the protocol and presentation of the study as follows: lack of controls or historic incidence data for the strain of rat used; unclear mineralogic classification of various samples, particularly numbers 4, 5 and 6; the small number of fiber and particle counts obtained for each sample may limit the accuracy of the size distributions reported; lack of knowledge concerning the representativeness of the non-asbestiform varieties used, and because of saturation doses causing maximal responses for three samples, dose-response relationships cannot be developed for these samples. NIOSH cautioned that because the study has been neither peer reviewed nor published, lacks controls, and has other defects, it should not be

relied upon by OSHA for any significant regulatory decision. (Ex. 532) Langer et al took issue with most of the NIOSH criticisms in their post hearing comments (Ex. 550). In particular they state that NIOSH is incorrect in its statement that the mineralogic classification of samples 4, 5 and 6 is unclear. Langer et al point out that the minerals were characterized by "continuous scanning X-ray diffraction, polarized light microscopy as well as scanning and transmission electron microscopy equipped with an energy dispersive X-ray spectrometer." They also disagree with NIOSH statements that "the small number of fiber and particle counts obtained for each sample may limit the accuracy of the size distribution reported." Langer et al note that "in each operation 300 fibers of all sizes were counted and measured..". and "to improve the statistical quality for long fibers the count was continued only for fibers >5 um... until 100 fibers > 5 um had been counted...this was done twice for most of the samples and three times for the Ala di Stura (i.e. Italian) and Dornie samples" ( Ex. 550, p. 7).

Dr. David Groth, a former NIOSH scientist, testifying on his own behalf, disagreed with statements made by Addison that the tumor incidence observed for the Dornie sample (12 percent) and the Shinness sample (5 percent) was within the background incidence for historical controls. Dr. Groth contends that this observation is not supported by the data published from Addison's lab. Dr. Groth states that "In two separate publications in 1986..using the same strain of rats (AF/HAN) in full life-span experiments no mesotheliomas were observed in 61 control rats in one experiment and 64 control rats in another experiment." (Ex. 529-1, p.2) In addition Dr. Groth cites several other results from Addison's lab which show no background incidence of mesothelioma for this strain of rat. Dr. Groth concludes the "the finding of peritoneal mesotheliomas in 6 percent of rats injected with the Shinness tremolite sample is a significant finding and provides further support for Stanton's theory regarding the carcinogenic potential of all fibers, including non-asbestiform fibers." (Ex. 529-2, p. 3).

According to Dr. Addison, a co-author of the study, "the results of the...study suggest that a wide ranging group of tremolite samples all possessed some potential to produce mesotheliomas following injection into the rat peritoneal cavity" and "In general carcinogenicity relates to the number of long thin fibers than to any of the other dimensional characteristics of the dusts that were considered but the relationship was by no means exact." (Ex. 479-22, p. 13). Dr. Addison added however that "the intraperitoneal injection test is, however, extremely sensitive and it is usually considered that, with a 10 mg dose, any dust which produces tumours in less than 10 percent of the experimental group is unlikely to show evidence of carcinogenicity following dust administration by the more natural route of inhalation". (Ex. 479-22, p. 14-15) He thus concluded that human exposure to such a material "will certainly produce no hazard."

Based on the record evidence, OSHA believes that the Davis et. al study confirms the view that various forms of tremolite have different pathogenic potential. For five of the six samples, constant relationships prevailed between asbestiform fibers and high potency and between non-asbestiform dusts and low potency. Interpreting the Italian sample is more problematic, and only speculative explanations exist for why it is more potent than would have been predicted based on its relatively small number of high aspect ratio fibers.

Other animal studies were the subject of testimony and comment, but the analyses essentially reiterated positions taken by the parties in communications to the Agency prior to the proposal. OSHA described the Smith study in its proposal as follows: "Smith et al injected four different talc samples intrapleurally into hamsters. The samples included fibrous tremolitic talc from New York State, tremolitic talc from the facility studied by NIOSH, tremolitic talc from the Western U.S. and asbestiform tremolite. Only the western talc and the asbestiform tremolite induced tumors in hamsters." (55 FR 4948).

Various mineralogic characterizations of the western talc have been made. Dr. Wylie, in cross-examination, reiterated her earlier characterization of the western talc, as a fibrous form of tremolite. Dr. Wylie further explained "it wasn't obviously only a sample of asbestos. I think I referred to it as byssolite." However because evidence of that sample consists of one photograph of that material, Dr. Wylie cautioned against drawing "too many conclusions ...about that one sample." (Tr. 5/9, p. 235.) OSHA agrees with Dr. Wylie and additionally notes that other deficiencies make the Smith study inconclusive. (See discussion in the preamble to the proposal, where OSHA noted the small number of animals, early death of many animals, lack of systematic characterization of fiber size and aspect ratio; 55 FR 4948).

The few additional animal studies undertaken to examine the toxicity of non-asbestiform ATA, either do not inform or do not show equivalent toxicity of ATA. The 1974 intraperitoneal injection rat study conducted by Pott et al, showed no tumor development for the animals injected with the primarily non-asbestiform actinolite sample (Ex. 479-6). The Cook studies of ferroactinolite fibers, show that the sample which was observed to undergo a higher degree of in vivo longitudinal splitting, resulted in more retained fibers, and in a higher concentration of retained fibers. Dr. Wylie noted that "(t)he durability of amphiboles in vivo is well known and the only way for this sample to break down into fibers of smaller widths is for separation of the fiber bundles to have occurred in vivo. They don't dissolve. Fiber bundles are the hallmark of asbestos and this characteristic is clearly revealed in the behavior of Coffin's ferroactinolite". (Tr. 5/9 at 104). Additional evidence was submitted in support of the view that the ferroactinolite sample was, in significant part, asbestiform. Thus, Dr. Lee concluded, based on his electron microscopic analysis, that as much as 61 percent of the sample may be asbestos with 33 percent existing as bundles (Ex. 490F Attach. A, p.2). OSHA concludes that it is more likely that the ferroactinolite sample that resulted in excess tumors is asbestiform and for that reason, the experimental results are not informative concerning the biological potential of non-asbestiform ATA.

OSHA believes that as a whole the animal experiments conducted confirm that for clearly differentiated dust populations, qualitative differences in carcinogenic potential exist between what is commonly considered "asbestos" and "cleavage fragments". Virtually all participants in this rulemaking agreed with this assessment. Even participants who endorsed regulation of non-asbestiform ATA as asbestos agreed that the longer, thinner fibers were more potent. (See Nicholson at Tr. 5/8, p. 60).

### c. Conclusions

Based on the rulemaking record before it, OSHA reaffirms its preliminary determination in the proposal that there is insufficient evidence to conclude that non-asbestiform ATA present a health risk similar in kind and magnitude to that of their asbestiform counterparts.

Asbestos is regulated as a carcinogen. Some health effects data relating to non-asbestiform ATA involved exposures to mixed mineral populations or particles which were poorly characterized such that no conclusions could be made regarding the carcinogenicity of non-asbestiform ATA. In other cases there were health effects data in humans, reportedly exposed to non-asbestiform ATA, which did not show excess cancer risks similar to those observed among animals and humans exposed to asbestos. However some of these data suffer from methodological deficiencies (e.g. low fiber exposure, poor animal survival and poor mineralogical characterization). These flaws may limit the studies' ability to detect the carcinogenic potential of non-asbestiform ATA if one is present. However, in many of the studies, asbestiform and non-asbestiform minerals were tested in the same experiment using the same protocol and only the asbestiform minerals induced a positive response. Thus, while the studies' results cannot be used to show that non-asbestiform ATA presents no carcinogenic risk, due to certain methodological flaws, the results from these studies do

suggest that if a carcinogenic risk does exist for non-asbestiform ATA, the risk is likely to be substantially less than that of asbestos. Given both the lower potency of any potential carcinogenic risk, and the high degree of uncertainty that would accompany any such estimate, OSHA believes the health effects evidence does not support treating non-asbestiform ATA as presenting a risk equivalent in kind or extent to asbestos.

In addition, OSHA finds that the evidence is insufficient to conclude that exposure to non-asbestiform ATA may result in a significant risk of nonmalignant respiratory disease (NMRD). Unquestionably, exposure to historic levels of tremolitic talc carried with it a significant risk of NMRD (i.e. pneumoconiosis). For example, studies by NIOSH, of tremolitic talc miners and millers in upstate New York (Ex. 84-181, Docket H-033c) have shown an excess risk for NMRD (SMR=280), among exposed workers. Similar findings of excess NMRD have also been observed in updated studies of this same group of workers both by NIOSH (SMR=250) and Gamble et al (SMR=251) (Exs. 532 and 478-8). Moreover NIOSH concluded in their update, that the observed excess in NMRD is more consistently associated with exposures at the mine. NIOSH's conclusion is based on their observation that a larger excess risk is observed among those employees with greater than one year employment at the mine (SMR=289) compared to those employees with less than one year employment at the mine (SMR=194). Even officials at the mine acknowledge the NMRD risk associated with the tremolitic talc. For example, in his testimony at the hearings, John Kelse, an industrial hygienist for the R.T. Vanderbilt Company, stated that "(t)he Company has long believed that excess exposure to our talc -- and indeed any talc or mineral dust, can result in pulmonary impairment. We have never claimed otherwise. Non-neoplastic respiratory disease has indeed occurred among our talc miners and to an alarming degree among those exposed prior to the advent of modern dust control systems. ..We have never denied this pneumoconiosis potential." (Tr. 5/11 at 4-104). Similarly, Dr. Brian Boehlecke, testifying as a medical expert for the R.T. Vanderbilt Company, stated: "So my conclusion is that there is a risk of pneumoconiosis from exposure to the type of talc mined and processed at Gouverneur Talc. I believe this is recognized and acknowledged by the company. " (Tr. 5/11 at 4-100).


However although exposures at the mine are attributed to the observed excess in NMRD among exposed workers, the data is insufficient to determine that the non-asbestiform tremolite is the causative agent. The tremolitic talc to which workers are exposed is composed of a variety of different minerals. The non-asbestiform tremolite, although a major constituent, is but one of those minerals. In addition, studies of workers exposed to talcs which do not contain non-asbestiform minerals, have also shown an excess risk of NMRD similar to the excess risk which has been observed among the New York State tremolitic talc workers. (See studies of Vermont Talc workers, Selevan et al; Ex. 479-4 Ex. A). Although the study is too imprecise to conclude that non-asbestiform minerals do not induce pulmonary disease, the study of the Vermont miners does suggest that some agent other than non-asbestiform minerals may be the causative agent in the induction of NMRD. Thus OSHA is unable to conclude that the non-asbestiform content in tremolitic talc is the etiologic agent of NMRD evident at high exposure levels. As a result, OSHA is also unable to conclude that non-asbestiform ATA presents a significant risk of NMRD.

[57 FR 24310, June 8, 1992]

---

 [Regulations \(Preambles to Final Rules\) - Table of Contents](#)

---

 [Back to Top](#)

[www.osha.gov](http://www.osha.gov)

[www.dol.gov](http://www.dol.gov)

---

[Contact Us](#) | [Freedom of Information Act](#) | [Customer Survey](#)

Occupational Safety & Health Administration  
200 Constitution Avenue, NW  
Washington, DC 20210